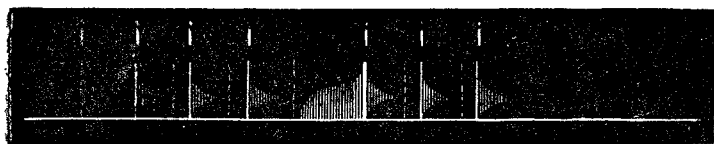


patient is placed under suitable conditions of rest and treatment (notably digitalis), and this is a favourable sign, as showing increased cardiac power.

In all these conditions (which I hope to be able to show you to-day) it is evident that there are many sources of error, because, though each one of them is marked by certain definite signs, it is clear that no one description can possibly include them all. When it is remembered that any one of these can be, and often is, complicated by mitral regurgitation or disease of the other valves—so that, for instance, an extreme case of mitral stenosis might be marked only by a sharp clicking first sound, no murmur, and no second sound; or, on the other hand, by a “systolic” murmur, without presystolic murmur or second sound,—it is not to be wondered at that assaults have been made on the very existence of the direct murmur—i.e., one caused by the flow of blood from auricle to ventricle, call it what you will, diastolic, presystolic, or auriculo-systolic.

A case remarkably illustrative of this condition is now attending as an out-patient (C. D—, No. 8297), in whom the cardiac rhythm is so irregular and the heart's action so feeble, that, though the heart beat is 152, the radial pulse is only 84. While standing up nothing can be heard over

FIG. 2.



the apex beat except a succession of short blowing whiffs, with no second sound. When lying down, every now and then as the heart gathers strength there is a pause, a hesitation, and then a long rolling presystolic murmur ending with a snap. (Fig. 2.)

(To be continued.)

NOTE ON

THE EFFECTS PRODUCED ON MAN BY SUBCUTANEOUS INJECTIONS OF A LIQUID OBTAINED FROM THE TESTICLES OF ANIMALS.

By DR. BROWN-SÉQUARD, F.R.S. &c.

ON the 1st of June last I made at the Société de Biologie of Paris a communication on the above subject, which was published in the *Comptes Rendus* of that Society on June 21st (No. 24). I will give here a summary of the facts and views contained in that paper and in two subsequent ones, adding to them some new points.

There is no need of describing at length the great effects produced on the organisation of man by castration, when it is made before the adult age. It is particularly well known that eunuchs are characterised by their general debility and their lack of intellectual and physical activity. There is no medical man who does not know also how much the mind and body of men (especially before the spermatogenic glands have acquired their full power, or when that power is declining in consequence of advanced age) are affected by sexual abuse or by masturbation. Besides, it is well known that seminal losses, arising from any cause, produce a mental and physical debility which is in proportion to their frequency. These facts and many others have led to the generally admitted view that in the seminal fluid, as secreted by the testicles, a substance or several substances exist which, entering the blood by resorption, have a most essential use in giving strength to the nervous system and to other parts. But if what may be called spermatogenic anæmia leads to that conclusion, the opposite state, which can be named spermatogenic plethora, gives as strong a testimony in favour of that conclusion. It is known that well-organised men, especially from twenty to thirty-five years of age, who remain absolutely free from sexual intercourse or any other causes of expenditure of seminal fluid, are in a state of excitement, giving them a great, although abnormal, physical and mental activity. These two series of facts contribute to show what great dynamogenic power is

possessed by some substance or substances which our blood owes to the testicles.

For a great many years I have believed that the weakness of old men depended on two causes—a natural series of organic changes and the gradually diminishing action of the spermatogenic glands. In 1869, in a course of lectures at the Paris Faculty of Medicine, discussing the influence possessed by several glands upon the nervous centres, I put forward the idea that if it were possible without danger to inject semen into the blood of old men, we should probably obtain manifestations of increased activity as regards the mental and the various physical powers. Led by this view, I made various experiments on animals at Nahant, near Boston (United States), in 1875. In some of those experiments, made on a dozen male dogs, I tried vainly, except in one case, to engraft certain parts or the whole body of young guinea-pigs. The success obtained in the exceptional case served to give me great hopes that by a less difficult process I should some day reach my aim. This I have now done. At the end of last year I made on two old male rabbits experiments which were repeated since on several others, with results leaving no doubt as regards both the innocuity¹ of the process used and the good effects produced in all those animals. This having been ascertained, I resolved to make experiments on myself, which I thought would be far more decisive on man than on animals. The event has proved the correctness of that idea.

Leaving aside and for future researches the questions relating to the substance or substances which, being formed by the testicles, give power to the nervous centres and other parts, I have made use, in subcutaneous injections, of a liquid containing a small quantity of water mixed with the three following parts: first, blood of the testicular veins;² secondly, semen; and thirdly, juice extracted from a testicle, crushed immediately after it has been taken from a dog or a guinea-pig. Wishing in all the injections made on myself to obtain the maximum of effects, I have employed as little water as I could. To the three kinds of substances I have just named, I added distilled water in a quantity which never exceeded three or four times their volume. The crushing was always done after the addition of water. When filtered through a paper filter, the liquid was of a reddish hue and rather opaque, while it was almost perfectly clear and transparent when Pasteur's filter was employed. For each injection I have used nearly one cubic centimetre of the filtered liquid. The animals employed were a strong and, according to all appearances, perfectly healthy dog (from two to three years old), and a number of very young or adult guinea-pigs. The experiments, so far, do not allow of a positive conclusion as regards the relative power of the liquid obtained from a dog and that drawn from guinea-pigs. All I can assert is that the two kinds of animals have given a liquid endowed with very great power. I have hitherto made ten subcutaneous injections of such a liquid—two in my left arm, all the others in my lower limbs—from May 15th to June 4th last. The first five injections were made on three succeeding days with a liquid obtained from a dog. In all the subsequent injections, made on May 24th, 29th, and 30th, and June 4th, the liquid used came from guinea-pigs. When I employed liquids having passed through Pasteur's filter, the pains and other bad effects were somewhat less than when a paper filter was used.

Coming now to the favourable effects of these injections, I beg to be excused for speaking so much as I shall do of my own person. I hope it will easily be understood that, if my demonstration has any value—I will even say any significance—it is owing to the details concerning the state of my health, strength, and habits previously to my experiments, and to the effects they have produced.

I am seventy-two years old. My general strength, which has been considerable, has notably and gradually diminished during the last ten or twelve years. Before May 15th last, I was so weak that I was always compelled to sit down after half an hour's work in the laboratory. Even when I

¹ This innocuity was also proved on a very old dog by twenty subcutaneous injections of a fluid similar to that I intended to employ on myself. No apparent harm resulted from these trials, which were made by my assistant, Dr. D'Arsonval.

² For reasons I have given in many lectures in 1869 and since, I consider the spermatogenic as also the principal glands (kidneys, liver, &c.) as endowed, besides their secretory power, with an influence over the composition of blood, such as is possessed by the spleen, the thyroid, &c. Led by that view, I have already made some trials with the blood returning from the testicles. But what I have seen is not sufficiently decisive to be mentioned here.

remained seated all the time, or almost all the time, in the laboratory, I used to come out of it quite exhausted after three or four hours' experimental labour, and sometimes after only two hours. For many years, on returning home in a carriage by six o'clock after several hours passed in the laboratory, I was so extremely tired that I invariably had to go to bed after having hastily taken a very small amount of food. Very frequently the exhaustion was so great that, although extremely sleepy, I could not for hours go to sleep, and I only slept very little, waking up exceedingly tired.³

The day after the first subcutaneous injection, and still more after the two succeeding ones, a radical change took place in me, and I had ample reason to say and to write that I had regained at least all the strength I possessed a good many years ago. Considerable laboratory work hardly tired me. To the great astonishment of my two principal assistants, Drs. D'Arsonval and Hénocque, and other persons, I was able to make experiments for several hours while standing up, feeling no need whatever to sit down. Still more: one day (the 23rd of May), after three hours and a quarter of hard experimental labour in the standing attitude, I went home so little tired that after dinner I was able to go to work and to write for an hour and a half a part of a paper on a difficult subject. For more than twenty years I had never been able to do as much.⁴ From a natural impetuosity, and also to avoid losing time, I had, till I was sixty years old, the habit of ascending and descending stairs so rapidly that my movements were rather those of running than of walking. This had gradually changed, and I had come to move slowly up and down stairs, having to hold the banister in difficult staircases. After the second injection I found that I had fully regained my old powers, and returned to my previous habits in that respect.

My limbs, tested with a dynamometer, for a week before my trial and during the month following the first injection, showed a decided gain of strength. The average number of kilogrammes moved by the flexors of the right forearm, before the first injection was about 34½ (from 32 to 37), and after that injection 41 (from 39 to 44), the gain being from 6 to 7 kilogrammes. In that respect the forearm flexors re-acquired, in a great measure, the strength they had when I was living in London (more than twenty-six years ago). The average number of kilogrammes moved by those muscles in London in 1863⁵ was 43 (40 to 46 kilogrammes).

I have measured comparatively, before and after the first injection, the jet of urine in similar circumstances—i.e., after a meal in which I had taken food and drink of the same kind in similar quantity. The average length of the jet during the ten days that preceded the first injection was inferior by at least one quarter of what it came to be during the twenty following days. It is therefore quite evident that the power of the spinal cord over the bladder was considerably increased.

One of the most troublesome miseries of advanced life consists in the diminution of the power of defecation. To avoid repeating the details I have elsewhere given in that respect, I will simply say that after the first days of my experiments I have had a greater improvement with regard to the expulsion of fecal matters than in any other function. In fact a radical change took place, and even on days of great constipation the power I long ago possessed had returned.

With regard to the facility of intellectual labour, which had diminished within the last few years, a return to my previous ordinary condition became quite manifest during and after the first two or three days of my experiments.

It is evident from these facts and from some others that all the functions depending on the power of action of the nervous centres, and especially of the spinal cord, were notably and rapidly improved by the injections I have used. The last of these injections was made on June 4th, about five weeks and a half ago. I ceased making use of

them for the purpose of ascertaining how long their good effects would last. For four weeks no marked change occurred, but gradually, although rapidly, from the 3rd of this month (July) I have witnessed almost a complete return of the state of weakness which existed before the first injection. This loss of strength is an excellent counter-proof as regards the demonstration of the influence exerted on me by the subcutaneous injections of a spermatic fluid.

My first communication to the Paris Biological Society was made with the wish that other medical men advanced in life would make on themselves experiments similar to mine, so as to ascertain, as I then stated, if the effects I had observed depended or not on any special idiosyncrasy or on a kind of auto-suggestion without hypnotisation, due to the conviction which I had before experimenting that I should surely obtain a great part at least of these effects. This last supposition found some ground in many of the facts contained in the valuable and learned work of Dr. Hack Tuke on the "Influence of the Mind over the Body." Ready as I was to make on my own person experiments which, if they were not dangerous, were at least exceedingly painful, I refused absolutely to yield to the wishes of many people anxious to obtain the effects I had observed on myself. But, without asking my advice, Dr. Variot, a physician who believed that the subcutaneous injections of considerably diluted spermatic fluid⁶ could do no harm, has made a trial of that method on three old men—one fifty-four, another fifty-six, and the third sixty-eight years old.⁷ On each of them the effects have been found to be very nearly the same as those I have obtained on myself. Dr. Variot made use of the testicles of rabbits and guinea-pigs.

These facts clearly show that it was not to a peculiar idiosyncrasy of mine that the effects I have pointed out were due. As regards the explanation of those effects by an auto-suggestion, it is hardly possible to accept it in the case of the patients treated by Dr. Variot. They had no idea of what was being done; they knew nothing of my experiments, and were only told that they were receiving *fortifying* injections. To find out if this qualification had anything to do with the effects produced, Dr. Variot, since the publication of his paper, has employed similar words of encouragement, whilst making subcutaneous injections of pure water on two other patients, who obtained thereby no strengthening effect whatever.⁸

I believe that, after the results of Dr. Variot's trials, it is hardly possible to explain the effects I have observed on myself otherwise than by admitting that the liquid injected possesses the power of increasing the strength of many parts of the human organism. I need hardly say that those effects cannot have been due to structural changes, and that they resulted only from nutritive modifications, perhaps in a very great measure from purely dynamical influences exerted by some of the principles contained in the injected fluid.

I have at present no fact to mention which might serve to solve the question whether it would be possible or not to change structurally muscles, nerves, and the nervous centres by making during a good many months frequent injections of the fluid I have used. As I stated at the Paris Biological Society, I have always feared, and I still fear, that the special nutritive actions which bring on certain changes in man and animals, from the primitive embryonal state till death by old age, are absolutely fatal and irreversible. But in the same way that we see muscles which have from disease undergone considerable structural alterations regain sometimes their normal organisation, we may, I believe, see also some structural changes not essentially allied with old age, although accompanying it, disappear to such a degree as to allow tissues to recover the power they possessed at a much less advanced age.

Whatever may be thought of these speculations, the

³ I ought to say that, notwithstanding that dark picture, my general health is and has been almost always good, and that I had very little to complain of, excepting mercism and muscular rheumatism.

⁴ My friends know that, owing to certain circumstances and certain habits, I have for thirty or forty years gone to bed very early and done my writing work in the morning, beginning it generally between three and four o'clock. For a great many years I had lost all power of doing any serious mental work after dinner. Since my first subcutaneous injections I have very frequently been able to do such work for two, three, and one evening for nearly four hours.

⁵ I have a record of the strength of my forearm, begun in March, 1860, when I first established myself in London. From that time to 1862 I occasionally moved as much as 50 kilogrammes. During the last three years the maximum moved was 38 kilogrammes. This year, previously to the first injection, the maximum was 37 kilogrammes. Since the injection it has been 44.

⁶ In my third communication at the Biological Society, I said that both the intense pain each injection has caused me and the inflammation it has produced would be notably diminished if the liquid employed were more diluted. The three cases of Dr. Variot have proved the exactitude of my statement. He made use of a much larger amount of water, and his patients had to suffer no very great pain and no inflammation.

⁷ The paper of Dr. Variot and my remarks upon it have appeared in the "Comptes Rendus de la Société de Biologie," No. 26, 5 Juillet, 1889, pp. 451 and 454.

⁸ Since writing the above I have received a letter from Dr. Variot announcing that, after injecting the liquid drawn from the testicles into these two individuals, he has obtained the same strengthening effects I have myself experienced.

results I have obtained by experiments on myself and those which have been observed by Dr. Variot on three old men show that this important subject should be further investigated experimentally.⁹

Brighton.

A CASE OF RAYNAUD'S SYMMETRICAL GANGRENE IN A PATIENT SUFFERING FROM CON- STITUTIONAL SYPHILIS.

WITH SOME REMARKS ON THE HISTORY, NATURE, AND
MANIFESTATIONS OF THE DISEASE.

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(Continued from page 66.)

RAYNAUD'S two contributions to this disease—his original thesis, published in 1862, and a supplementary paper written twelve years later, in 1874—contain a record of thirty-one cases. The mean age of the patients he refers to is 27·7 years. Twenty-two of his cases were females and nine males. Five of the sufferers were children between three and nine years of age. As I have already stated, I have myself collated ninety-three cases, which correspond more or less closely with the description given by Raynaud. I have omitted all examples of the disease in which the symptoms seemed due to organic changes in the heart and in the vessels; also numerous other cases which appeared to depend on diabetes or ergot of rye; and likewise others where the malady might be looked upon as one of the sequelæ of some protracted wasting disorder, such as typhoid fever, associated with thrombosis of the veins of the lower extremities. In these ninety-three cases the mean age of the patients was 26·6, a number which very nearly corresponds with the mean age of Raynaud's cases. Still, my statistics do not support his statement that females between eighteen and thirty are most liable to be affected. My tables go to show that the disorder is pretty evenly distributed between the different decades of life up to sixty years of age; indeed, if there be any period of life when it is especially prone to occur, it is in very early childhood. Thus, in no fewer than thirteen of my cases the age of the patient ranged from two and a half to five years, eleven from five to ten years, fifteen from ten to twenty years, sixteen from twenty to thirty years, fifteen from thirty to forty years, thirteen from forty to fifty years, and ten from fifty to sixty years. Doubtful cases of the disorder have been described in two young infants; but in the youngest well-authenticated example of the disorder the age was two years and a half, the oldest fifty-nine. Of the ninety-three cases, fifty-four were females and thirty-nine males; thus the proportion of males to females in my tables was very much greater than appears from Raynaud's statistics. The numerous examples of the disease recorded in early childhood is somewhat remarkable, no fewer than twenty-four of the ninety-three sufferers being under ten years of age. In early life, as is well known, the sympathetic system, as distributed to the abdominal organs, is peculiarly susceptible to disturbing influences, and many of the cases observed among the very young proved singularly grave in their progress and in their consequences; indeed, it is among these little patients that we meet with examples of gangrene which may be described as the acute and malignant form of the disorder. The child perhaps has died in thirty or forty hours, while the progress of the disease has been continuously from bad to worse. Here there is nothing paroxysmal about the attack; the symptoms progress uninterruptedly and terminate fatally. Such a case was brought before the Pathological Society of London¹ by Dr. Southey. He showed the body of a child, aged two years and a half. On Dec. 2nd livid patches were noticed on the back of the calves; they

got blacker, and extended over the legs; the backs of the arms were similarly affected. The buttocks next got livid. The lesions were symmetrical; the child was seized with convulsions and died. She was ill for thirty-two hours only. In another case, reported by Mr. A. D. Murray,² a boy aged three was taken ill on March 5th; both feet became black and gangrenous; in an hour the hands and arms were dusky; on the 6th a discoloured patch was observed on the back of the left thigh, and in the afternoon one on the left cheek; the patient died at 10 P.M., being ill for two days only. Dr. Tannahill also refers to a case in which a child similarly affected died thirty-six hours after its admission into hospital; while Mr. E. Bellamy has described one in a child aged four, in which death occurred on the fourth day. Other cases have been recorded in which the disorder assumed an equally grave character, though the symptoms were far more protracted; as, for example, in Mr. Solly's case, where all the extremities were lost, and the patient eventually died. Similar examples of the disease have been reported by Mr. Thomas Smith, M. Bocquet, Dr. Grayhill, and others, all occurring in very young children, and tending to show how destructive in its effects symmetrical gangrene may prove when it invades the system of the very young. In Raynaud's original thesis, he dwells with marked emphasis on the numerous instances in which he has found this variety of gangrene associated with irregularity of the menstrual functions in young women; indeed, he distinctly asserts that the most frequent exciting cause is suppression of the menses. This opinion was disputed by Vulpian, whose observations are strikingly confirmed by my own tables, which conclusively show that in very few instances was any irregularity observed in the catamenia. Indeed, in several of the most characteristic cases, it is distinctly stated that the monthly period exercised no special influence over the symptoms of the disease. In alluding to this variety of gangrene, the distinguished discoverer of the disease remarks: "The nose and the external ears are sometimes more or less attacked. I am not aware, however, that in these situations complete mortification has been observed." Both before and since Raynaud's investigations were published several cases have been recorded where these organs were at least partially destroyed by the gangrenous processes. Thus, Mr. J. D. Nott³ observes, in reference to a patient of his, a boy aged ten, "the tip of the nose and the ears and the lips dried and dropped off, leaving the surface underneath healthy." So, again, Mr. J. R. Bigg wrote to THE LANCET in 1870 regarding a delicate woman suffering from symmetrical gangrene, and stated that forty days after the commencement of the symptoms it was necessary to remove the tip of the nose, and portions of both ears. Mr. Clifford Beale⁴ also speaks of a considerable part of the helix in both ears as being wanting, in consequence of the ravages of this disease. In Mr. Grindall's case, also, the nose was entirely destroyed by mortification; and it was further observed that in my patient a considerable portion of the helix of the right ear sloughed away, part of the cartilage of the ear being at the same time destroyed. In considering the outward manifestations of this curious neurosis, it will be instructive to recall the different parts of the body in which symmetrical patches are said to have occurred coincidentally with the disturbed state of the circulation in the extremities. Indeed, had not either toes, fingers, ears, or nose been simultaneously affected, it would not, from our present standpoint, have been permissible to speak of these lesions as an integral portion of Raynaud's disease. In the first place, they are in the vast majority of cases met with in those portions of the trunk and limbs in which each side of the body has its corresponding counterpart on the other side—parts to which the term "homologous" may appropriately be applied. In several instances patches were observed over the heels, over the calves, over the malleoli, and over the tibiæ. In numerous cases the whole of the lower extremities were involved. In others a purple patch was seen on each side of the umbilicus. In several more the nates were involved; in some, various portions of the back; in some, the cheeks and lips. Petri has described how curiously he himself was affected; some of the patches on his own body appearing over the deltoid muscles on the outer surface of the arms, others over the clavicles, and others, again, over the situation of the medial nerve, a few inches above the wrist;

⁹ It may be well to add that there are good reasons to think that subcutaneous injections of a fluid obtained by crushing ovaries just extracted from young or adult animals, and mixed with a certain amount of water, would act on old women in a manner analogous to that of the solution extracted from the testicles injected into old men.

¹ Brit. Med. Jour., Dec. 9th, 1882.

² Ibid., vol. i., p. 70.

³ Prov. Med. and Surg. Jour., 1846.

⁴ Brit. Med. Jour., vol. i. 1887.